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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/374,967	08/16/1999	KANWARPAL S. DHUGGA	5718-55	4392

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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 06/02/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/374,967	DHUGGA ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,9,10,12,23,32,41-45 and 77-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,9,10,12,23,32,41-45 and 77-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1, 3-4, 7-8, 11, 13, 24 and 33 have been cancelled, claims 5, 23, 32 and 45 have been amended, and claims 77-81 have been added as requested in Paper No. 19, filed 26 March 2003. Claims 5, 9-10, 12, 23, 32, 41-45 and 77-81 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment

3. The objection to claim 11 is obviated by its cancellation.

4. The rejection of claim 45 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is WITHDRAWN in light of amendment to indicate that the seed is transformed.

5. The rejection of claims 23, 32 and 41-45 under 35 U.S.C. 103(a) as being unpatentable over each of Gordon-Kamm et al (1990, Plant Cell 2:603-618) and Facciotti et al (1985, BioTechnology 3:241-246) in view of Hashimoto et al (1997, J. Biol. Chem. 272:16308-16314), further in view of Wheeler et al (1998, Nature 393:365-369) is WITHDRAWN in light of amendment to make the claims dependent upon claim 77.

Claim Rejections - 35 USC § 112

6. Claims 5, 9-10, 12, 23, 32, 41-45, 77-78 and 81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO:1, does not reasonably provide enablement for a multitude of nucleic acids that encode maize or

legume GDP-mannose pyrophosphorylase, that encode SEQ ID NO:2, that have 90% identity to SEQ ID NO:1, or that encode an antisense RNA of one of those nucleic acids, and plants transformed with those nucleic acids in a sense or antisense orientation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as set forth in the Office action mailed 21 November 2002, as applied to claims 1, 3-5, 7-13, 23-24, 32-33 and 41-45. Applicant's arguments filed 26 March 2003 have been fully considered but they are not persuasive.

Applicant urges that the claims have been amended to be dependent upon claim 77. Applicant urges that GDP-mannose pyrophosphorylase sequences are well-known in the art; thus, one of skill in the art can make and use the nucleic acid of claim 77, Applicant also urges that guidance for determining percent identity is present in the specification and that generating such nucleic acids is routine, and methods of assaying GDP-mannose pyrophosphorylase are routine. Applicant thus urges that one of skill in the art could make and test modified variants of the sequences, and doing so would not require undue experimentation (response pg 5-7).

This is not found persuasive. The rejection is not for making a nucleic acid with 90% identity to SEQ ID NO:1; the rejection is for making such a nucleic acid wherein the nucleic acid encodes a GDP-mannose pyrophosphorylase. The specification does not teach the critical amino acids for maize GDP-mannose pyrophosphorylases and does not teach which amino acids can tolerate substitutions. Thus, making the claimed nucleic acid would require trail and error experimentation, and given the huge number of possible variants (for example, 19^{361} ones with 99.7% similarity), doing so would require undue experimentation.

See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Applicant urges that the specification on pg 9-12 provides guidance for primers, probes and hybridization (response pg 7).

This is not found persuasive because these pages do not provide guidance for the specific probes and primers and hybridization conditions required to isolate the claimed sequences but only provide general guidance for hybridization, probes and primers.

Applicant urges that the present claims exclude non-operative embodiments and that the specification cites Dayhoff et al for guidance and states that conservative substitutions may be preferred. Applicant urges that screening the nucleic acid would not be undue experimentation and GDP-mannose pyrophosphorylase are taught (response pg 7-9).

This is not found persuasive. The specification does not teach which amino acids of SEQ ID NO:2 are critical for function and which may be altered, and to what other amino acids. Given the lack of guidance presented in the specification, one must use trail and error experimentation to make and assay the claimed nucleic acids. Dayhoff et al could not considered because it was not sent.

Applicant urges that the Examiner's concern that the specification does not recite exact hybridization conditions, specific PCR, critical sequence motifs and functional assays is incorrect or unwarranted. Applicant urges that Hashimoto teaches conserved motifs in Figure 4,

that GDP-mannose pyrophosphorylase assays are taught on pg 17-18 of the specification, and that hybridization, and PCR are taught on pg 9 and 11-12 (response pg 10).

This is not found persuasive. The proteins shown in Figure 4 of Hashimoto et al are not, as Applicant suggests, all GDP-mannose pyrophosphorylases but are simply sugar pyrophosphorylases. Only one of the proteins shown in Figure 4 is GDP-mannose pyrophosphorylases (see the paragraph spanning pg 16310-16311 for an explanation). Thus, Hashimoto et al does not teach conserved motifs of GDP-mannose pyrophosphorylases.

Furthermore, Hill et al, cited in the prior Office action, teach that using amino acid alignment for making amino acid substitutions is unreliable. ADP-glucose pyrophosphorylase has three histidines that are maintained across several species; it would be "expected" that these positions could tolerate no or only conservative amino acid substitutions. However, when they are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). Thus, alignment of an enzyme from several sources cannot provide guidance for making nucleic acids with 90% identity to SEQ ID NO:1 and that encode a protein with that enzymatic activity.

The cited pages of the specification do not provide guidance for the specific probes and primers and hybridization conditions required to isolate the claimed sequences but only provide general guidance for hybridization, probes and primers.

7. Claims 5, 9-10, 12, 23, 32, 41-45, 77-78 and 81 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 21 November 2002, as applied to claims 1, 3-5, 7-13, 23-24, 32-33 and 41-45. Applicant's arguments filed 26 March 2003 have been fully considered but they are not persuasive.

Applicant urges that GDP-mannose pyrophosphorylases comprise a well-characterized protein family that at the time of filing had been characterized at the functional and structural level. Applicant urges that Hashimoto et al, in Figure 4, teaches the structural motifs common to members of this genus (response pg 11-12).

This is not found persuasive because, as discussed above, the proteins shown in Figure 4 of Hashimoto et al are not all GDP-mannose pyrophosphorylases but are simply sugar pyrophosphorylases. Only one of the proteins shown in Figure 4 is GDP-mannose pyrophosphorylases (see the paragraph spanning pg 16310-16311 for an explanation). Thus, Hashimoto et al does not teach structural motifs of GDP-mannose pyrophosphorylases.

Applicant urges that the functional characteristics of GDP-mannose pyrophosphorylases are known in the art; the reaction catalyzed by GDP-mannose pyrophosphorylases is described in the specification. Applicant urges that Hashimoto et al also teaches assays for GDP-mannose pyrophosphorylases (response pg 12).

This is not found persuasive because written description requires structural and functional description, and a structural description is missing in the instant case. The specification does not describe the structural features, (*i.e.*, sequence) of a nucleic acid that encodes other maize GDP-mannose pyrophosphorylases or nucleic acids that have 90% identity to SEQ ID NO:1 and encode a GDP-mannose pyrophosphorylase.

Applicant urges that members of the GDP-mannose pyrophosphorylase protein family are well-characterized functionally and structurally and that recitation of 90% sequence identity is a very predictable structure. Applicant also urges that claim 77 recites that the claimed sequence encodes a protein that has GDP-mannose pyrophosphorylase activity in a plant or plant cell. Applicant thus urges that the claimed sequences are defined by relevant identifying physical and chemical properties (response pg 12-13).

This is not found persuasive because the rejection is not against description of nucleic acid with 90% identity to SEQ ID NO:1; the rejection sates that description of such a nucleic acid wherein the nucleic acid encodes a GDP-mannose pyrophosphorylase is lacking. Claim 77 does not recites that the claimed sequence encodes a protein that has GDP-mannose pyrophosphorylase activity in a plant or plant cell, and such a recitation would not describe the structural features of the claimed nucleic acid.

Applicant urges that *Univ. of California v. Eli Lilly* is improperly applied; the decision there turned on the conclusion that the patent lacked sufficient information on the relevant structural and physical characteristics of a cDNA, but did not exclude the possibility of claiming a genus of DNA molecules. Applicant urges that a genus may be described by recitation of a representative number of DNAs falling within the scope of the genus. Applicant urges that the Written Description Guidelines states that possession may be shown in many ways and that factors relevant to that determination include a number of characteristics (response pg 14-15).

This is not found persuasive because *Univ. of California v. Eli Lilly* states on pg 1406:

> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

Thus, description of one DNA, as in the instant case, is not each to recitation of a representative number of DNAs falling within the scope of the genus, even though insulin itself was well-characterized long before cloning any DNA that encodes it.

Applicant urges that written description requires the knowledge and level of [one] of skill in the art and cites *Purdue Pharma.* (response pg).

This is not found persuasive. *Purdue Pharma* states that inquiry into whether a case means the written description requirement "is a factual one and must be assessed on a case-by-case basis" (pg 1483). Furthermore, the case is drawn to the written description support for a specific limitation within a range and is thus not relevant to the instant case.

8. Claims 5, 9-10, 12, 23, 32, 41-45 and 77-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is modified from the rejection set forth in the Office action mailed 21 November 2002, as applied to claims 3-4 11 and 32-45, due to amendment of the claims. Applicant's arguments filed 26 March 2003 do not apply to these new rejections.

Claim 77, part (d), and claim 78, are indefinite in their recitation of "having GDP-mannose pyrophosphorylase activity" as the phrase modified "nucleotide sequence". A nucleotide sequence does not have GDP-mannose pyrophosphorylase activity, although a protein encoded by the sequence may.

9. Claims 5, 9-10, 12, 23, 32, 41-45 and 77-81 are free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid that encodes a maize GDP-mannose pyrophosphorylase, that encode SEQ ID NO:2, or that have 90% identity to SEQ ID NO:1, and plants transformed with those nucleic acids.

10. Claims 79-80 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0198.

Anne R. Kubelik, Ph.D.
May 21, 2003

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